Poly- L- lactic acid

Brand Name: Sculptra, New-Fill
Drug Class: Opportunistic Infection and Other Drugs

Drug Description

Poly-L-lactic acid (PLLA) is a biocompatible, biodegradable, and immunologically inert synthetic polymer from the alpha-hydroxy-acid family. [1] Microparticles of PLLA are the active ingredient in the injectable implant for treatment of facial atrophy. [2]

HIV/AIDS-Related Uses

PLLA was approved by the FDA on August 3, 2004, for the restoration and correction of the signs of facial fat loss in people with HIV.[3] Facial wasting is a common and disfiguring side effect of highly active antiretroviral therapy (HAART). Both nucleoside analogues and protease inhibitors are associated with the development of lipoatrophy.[4]

PLLA was approved in 1999 in Europe, under the brand name New-Fill, for the cosmetic treatment of wrinkles and has been used by an estimated 100,000 people. Dermik Laboratories, the Pennsylvania-based division of Aventis Pharmaceuticals Inc., filed with the FDA for premarket approval of PLLA in the United States under the brand name Sculptra.[5] On March 25, 2004, the FDA's General and Plastic Surgery Devices Advisory Panel recommended conditional approval for Sculptra for the treatment of HIV-associated lipoatrophy. Conditions for use in the U.S. include a physician training program, a postmarket study enrolling women and people of color, clear labeling with warnings against off-label use, and a description of the product as having a reconstructive rather than a cosmetic purpose. Such strong labeling conditions would greatly reduce the adverse events reported in 3 previous U.S. trials and discourage off-label use in HIV uninfected people.[6]

Non-HIV/AIDS-Related Uses

PLLA was approved in Europe in 1999 for the cosmetic correction of scars and wrinkles. PLLA is currently used in a variety of orthopedic and maxillofacial applications.[7]

Pharmacology

PLLA is the only treatment approved to correct sunken cheeks, hollow eyes, indentations, and other signs of facial fat loss, a common side effect of antiretroviral therapy for HIV. PLLA is injected into and around the deep dermis. The injections provide a gradual and significant increase in skin thickness, improving the appearance of folds and sunken areas.[8] A study of 50 HIV infected patients with severe facial atrophy reported mean increases in facial total cutaneous thickness (TCT) of 6.8 mm at 96 weeks, and 43% of patients had a facial TCT greater than 10 mm at 96 weeks. Patients in the study received three, four, or five sets of PLLA injections. The progressive increase in dermal thickness is thought to result from a local reaction followed by a progressive increase in collagen deposition. The bioactive material is degraded and safely undergoes resorption. While PLLA injections are associated with an increase in TCT, there is no increase in subcutaneous fat.[9] For most people who participated in PLLA clinical studies, the treatment results lasted for up to two years after the first treatment session.[10]

Adverse Events/Toxicity

PLLA injection has been associated with some adverse effects. In 5 clinical studies of HIV infected patients, no major adverse events were reported. Mild to moderate adverse events included bruising and hematoma related to injection.[11] The most common device-related adverse event was delayed occurrence of subcutaneous papules, which were confined to the injection site and were typically palpable, asymptomatic, and non-visible.[12] Side effects reported at the March 25, 2004 meeting of the FDA's General and Plastic Surgery Devices Advisory Panel included discomfort, bruising, edema, hematoma, inflammation, and erythema at the injection site.[13]

Post-injection, all patients had some degree of edema. A large proportion of patients (77%) experienced pain during the injection procedure, with about 28% of these requiring pain medication. About 13% of patients had post-injection

Poly- L- lactic acid

Adverse Events/Toxicity (cont.)

non-inflammatory nodules or papules. Severe side effects observed in limited clinical trials of PLLA included vagal hypertonia and lightheadedness (7.5%), inflammatory nodule development (1%), facial palsy upon hitting the facial nerve during treatment (1%), and anaphylaxis (1%).[14]

Drug and Food Interactions

No studies of interactions with PLLA with drugs or other substances or implants have been done.[15]

Contraindications

PLLA should not be used in any person who has hypersensitivity to any of the components of the product.[16]

Clinical Trials

For information on clinical trials that involve Poly-L-lactic acid, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Poly-L-lactic acid AND HIV Infections.

Dosing Information

Mode of Delivery: Injection.[17]

Dosage Form: Clear glass vials containing freeze-dried preparation for injection sealed with a penetrable stopper and covered by an aluminum seal with a flip-off cap.[18] Lyophilisate is to be reconstituted in 3 ml of sterile water and injected using a 26-gauge needle.[19]

Storage: PLLA injection can be stored at room temperature, up to 30 C (86 F). Do not freeze; refrigeration is not required.[20]

Chemistry

Molecular weight: 40 to 50 kDa[21]

Stability: Each vial of PLLA for injection is packaged for single-use only; do not resterilize.[22]

PLLA is physically, chemically, and microbiologically stable for up to 72 hours after reconstitution[23] [24] and up to two years as a lyophilisate.[25]

Other Names

PLA[26]

PLLA[27]

Further Reading

Berry J. New-Fill for an old face. Posit Aware. 2002 May-Jun;13(3):34-5. PMID: 12154742

Berger DS. New facial filling treatment for lipodystrophy. Posit Aware. 2001 Sep-Oct;12(5):17-20. PMID: 11688478

Moyle GJ, Lysakova L, Brown S, Sibtain N, Healy J, Priest C, Mandalia S, Barton SE. A randomized open-label study of immediate versus delayed polylactic acid injections for the cosmetic management of facial lipoatrophy in persons with HIV infection. HIV Med. 2004 Mar;5(2):82-7. PMID: 15012646

Valantin MA, Aubron-Olivier C, Ghosn J, Laglenne E, Pauchard M, Schoen H, Bousquet R, Katz P, Costagliola D, Katlama C. Polylactic acid implants (New-Fill) to correct facial lipoatrophy in HIV-infected patients: results of the open-label study VEGA. AIDS. 2003 Nov 21;17(17):2471-7. PMID: 14600518

Manufacturer Information

Poly-L-lactic acid
Dermik Laboratories, Inc.
1050 Westlakes Dr.
Berwyn, PA 19312
(484) 595-2700

Sculptra
Dermik Laboratories, Inc.
1050 Westlakes Dr.
Berwyn, PA 19312
(484) 595-2700

Poly- L- lactic acid

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

1. AIDS - 2003 Nov 21;17(17):2471-7

2. Dermik Laboratories - Sculptra Prescribing Information, p. 1. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

3. Dermik Laboratories - FDA Approves Sculptra. Available at: http://www.sculptra.com/US/resources/pr_20040803.pdf. Accessed 08/05/04.

4. AIDS - 2003 Nov 21;17(17):2471-7

5. FDA - Brief Summary From the General and Plastic Surgery Devices Panel Meeting. Available at: http://www.fda.gov/cdrh/panel/summary/gpsd-032504.html. Accessed 08/05/04.

6. Clinical Care Options for HIV - New-Fill Recommended for Approval in U.S. as Sculptra. Available at: http://clinicaloptions.com/hiv/news/news_NAM_259.asp. Accessed 08/05/04.

7. AIDS - 2003 Nov 21;17(17):2471-7

8. Dermik Laboratories - FDA Approves Sculptra. Available at: http://www.sculptra.com/US/resources/pr_20040803.pdf. Accessed 08/05/04.

9. AIDS - 2003 Nov 21;17(17):2471-7

10. Dermik Laboratories - FDA Approves Sculptra. Available at: http://www.sculptra.com/US/resources/pr_20040803.pdf. Accessed 08/05/04.

11. FDA - Brief Summary from the General and Plastic Surgery Devices Panel Meeting. Available at: http://www.fda.gov/cdrh/panel/summary/gpsd-032504.html. Accessed 08/05/04.

12. FDA - Sculptra Prescribing Information, p. 4. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

13. FDA - Sculptra Prescribing Information, pp. 3-4. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

14. Natl AIDS Treatment Advocacy Project (NATAP) - Report 2 on Sculptra (New-Fill): FDA Study Review; Advocacy Issues. Available at: http://www.natap.org/2004/HIV/032904_02.htm. Accessed 08/05/04.

15. FDA - Sculptra Prescribing Information, p. 2. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

16. FDA - Sculptra Prescribing Information, p. 1. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

17. Dermik Laboratories - Sculptra Prescribing Information, p. 1. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

18. Dermik Laboratories - Sculptra Prescribing Information, p. 7. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

19. FDA - General and Plastic Surgery Devices Panel Meeting, 03/25/04. Available at: http://www.fda.gov/ohrms/dockets/ac/04/transcripts/4031t1.htm. Accessed 08/05/04.

20. Dermik Laboratories - Sculptra Prescribing Information, p. 10. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

21. Natl AIDS Treatment Advocacy Project (NATAP) - Report 2 on Sculptra (New-Fill): FDA Study Review; Advocacy Issues. Available at: http://www.natap.org/2004/HIV/032904_02.htm. Accessed 08/05/04.

22. Dermik Laboratories - Sculptra Prescribing Information, p. 11. Available at: http://www.sculptra.com/US/resources/SculptraPI.pdf. Accessed 08/05/04.

23. Natl AIDS Treatment Advocacy Project (NATAP) - Report 2 on Sculptra (New-Fill): FDA Study Review; Advocacy Issues. Available at: http://www.natap.org/2004/HIV/032904_02.htm. Accessed 08/05/04.

24. FDA - General and Plastic Surgery Devices Panel Meeting, 3/25/04. Available at: http://www.fda.gov/ohrms/dockets/ac/04/transcripts/4031t1.htm. Accessed 08/05/04.

25. FDA - General and Plastic Surgery Devices Panel Meeting, 3/25/04. Available at: http://www.fda.gov/ohrms/dockets/ac/04/transcripts/4031t1.htm. Accessed 08/05/04.

26. AIDS - 2003 Nov 21;17(17):2471-7

27. AIDS - 2003 Nov 21;17(17):2471-7